controversial. Several reports have now confirmed that patients with residual disease measuring less than 2 cm exhibit a higher rate of complete remission and a longer duration of survival than patients with bulky residual masses. Those who question the value of an aggressive surgical approach argue that a fundamental difference in tumor biology is responsible for the unfavorable prognosis in patients with bulky residual masses.

The resection of bulky abdominal disease poses a formidable challenge even to the most experienced and skillful surgeon. For this reason, it has been possible to achieve "optimal" cytoreduction in no more than 40% to 70% of cases. The results of a recent study offer some hope of improving these figures. In nine of ten elderly patients, an ultrasonic surgical aspirator was used to achieve cytoreduction of bulky peritoneal metastases to less than 0.5 cm. Procedures involving the aspirator took less than half the time required for conventional surgical techniques. Bowel resection was avoided in all but one patient, and no operative complications were attributed to the use of the device.

For many years, the primary focus of research in ovarian cancer has been the development of a more effective chemotherapeutic regimen for patients with advanced disease. Several prospective, randomized trials have now shown that the intravenous administration of cisplatin in combination with cyclophosphamide constitutes the most effective treatment for these patients. Chemotherapeutic regimens containing the two drugs have yielded objective response rates of 60% to 80%, complete response rates of 30% to 40%, and a median survival of 24 to 30 months. The addition of Adriamycin (doxorubicin hydrochloride) or other agents does not appear to enhance the effectiveness of the two-drug combination.

In patients with persistent disease at a second laparotomy, the likelihood of a response to additional intravenous chemotherapy is less than 20% and the median survival is only six months. Ovarian cancer, however, is uniquely suitable for an alternative approach to drug administration. The direct intraperitoneal instillation of a chemotherapeutic agent exposes residual tumor nodules to an extremely high drug concentration as compared with systemic levels, making it possible in theory to enhance the drug's therapeutic index. In a recent study of intraperitoneal chemotherapy for residual disease at a second laparotomy, a cisplatin-based combination yielded a median survival of more than four years in patients whose disease measured less than 2 cm. Unfortunately, patients with more extensive residual disease did not benefit to the same degree.

Localized ovarian cancer is usually asymptomatic. Until recently, the only potential screening test for asymptomatic disease was a vaginal examination. Discovery of the CA-125 antigen and improvements in the technique of real-time ultrasonography have raised the possibility that an effective program for early detection can be developed. The CA-125 antigen is a glycoprotein that is expressed by more than 80% of nonmucinous epithelial ovarian cancers. Real-time ultrasonography is an accurate method of measuring ovarian volume.

In a recent study to determine the feasibility and specificity of multimodal screening, serum CA-125 levels were determined in 1,010 postmenopausal women. Ovarian ultrasonography, a less specific and more expensive test, was carried out in the 30 women with CA-125 levels greater than 30 units per ml. Only three of these women with elevated CA-125 levels had abnormal ultrasound scans. One of them was found to have stage I ovarian cancer, while the other two proved to have benign pelvic abnormalities. The specificity of the multimodal screening program was therefore 99.8%. To determine whether such a screening program is of real value would first require additional studies to define the sensitivity in patients with localized disease. Ultimately, it would be necessary to do a randomized, controlled trial to show a reduction in mortality.

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Topical Retinoic Acid, Aging, and the Skin

AMERICANS ARE CONTINUALLY BARRAGED by commercial images that promote gnawing anxiety about the normal consequences of aging. A disproportionate share of this dissatisfaction has focused on the perceived ravages of aging on the skin and its appendages. Much of this attention has been useful; for example, an increased use of sunscreens should slow the alarming recent increase in cases of skin carcinoma and melanoma. On the other hand, much of the anxiety about aging is not endogenous but fueled by aggressive marketing targeted at a population evermore dependent on passively received, idealized images for its perception of normal. Whether this has been beneficial is certainly debatable, particularly if the price is despair and depression. Physicians, traditionally the last bastion of skepticism and independent thinking, likewise are becoming increasingly dependent on passively dispensed information—videocassettes, direct mail advertising, drug company-sponsored speakers, and throwaway journals compiled by nonmedical journalists—because they, too, are part of a society that reads and thinks less. By obtaining their information through these routes, physicians knowingly or unwittingly become salespeople, themselves extensions of a marketing network, corrupting their primary responsibility as patients' advocates.

Nevertheless, the phenomenon is upon us. Where before monarchs, poets, and commoners alike awaited their death knell from an early age with each serious illness, we can now reasonably expect longevity, while at the same time our skin will increasingly be besieged by the electromagnetic consequences of a careless disregard of a deteriorating atmosphere and increased sun exposure due to expanded leisure time and Sunbelt migration patterns.

A veritable smorgasbord of cutaneous offerings awaits those in search of the font of youth: body recontouring by removal (plastic surgery or liposuction), or augmentation (collagen, fat, or silicon implantation), hair-growth potions of still-unproven value, "cosmetics of the future," and topical retinoids. Although all of these approaches merit separate examination of their relative virtues and demerits, it seems

particularly timely to discuss topical retinoic acid (tretinoin; Retin-A) in view of the recent, carefully managed spate of publicity surrounding this agent.

Is there solid evidence for its usefulness? Can physicians delineate specific indications for its use? Retinoic acid, the progenitor of several generations of synthetic retinoids,[1] exerts powerful effects on epidermal differentiation. By normalizing keratinocyte maturation, this agent can reverse and prevent preneoplastic changes, but only a few established skin cancers respond to either systemic or topical retinoids.[2]

Although the driving force for the development of the synthetic retinoids is the excessive toxicity of vitamin A and its derivatives, ironically, it may be the low-grade irritancy of retinoic acid that promotes its percutaneous delivery to the dermis, allowing this agent to exert its effects on mesenchymal elements in that layer. By stimulating fibroplasia, leading to de novo collagen and proteoglycan synthesis, retinoic acid displaces downward actinically damaged, elastotic collagen.[3] In addition to its effects on keratinocytes and fibroblasts, topical retinoic acid apparently can stimulate endothelial cell proliferation and pigment dispersal,[4] effects that also can improve the appearance of photodamaged skin. Retinoic acid has been appreciated longest for its impact on pilosebaceous structures: in addition to diminishing sebum output, retinoic acid may reduce the number of open and closed comedones. The former, in particular, are an additional stigmatum of photodamaged skin. Finally, in altering epidermal differentiation and accelerating shedding, topical retinoic acid can reduce much of the excess scale that can be a concomitant of aging skin. In fact, retinoids remain the most effective form of therapy for the ichthyoses,[5] a broad group of inherited and acquired disorders characterized by excess scale.[6]

Is topical retinoic acid a panacea for photoaging? Certainly not. The impact on extensively damaged, deeply furrowed skin is minimal. But the ability of this agent to reverse and prevent epidermal neoplasias—albeit not as effectively as 5-fluorouracil; stimulate the renewal of various cellular elements in the dermis; promote normal pigmentation; and reduce both excessive scale and follicular cornified material makes this agent, and perhaps generations of topical retinoids still to come, reasonable therapy for extensively photodamaged skin. Finally, there are obvious advantages to medical versus surgical therapy for extensively sun-damaged skin, although the use of topical retinoids does not preclude, and even may complement, such surgical interventions as dermabrasion, chemical peels, and collagen implantation.

Topical retinoids also hold promise as primary and adjunctive therapy for a variety of other cutaneous processes, including enhancing the healing of leg ulcers in patients receiving systemic steroids or nonsteroidal anti-inflammatory agents, reversing dysplastic changes in dysplastic nevi, treating a variety of mucosal ulcerative and scarring conditions, and stimulating hair growth. Much of this work is still preliminary and beyond the scope of this article but available to readers in two recently published symposia.[7,8]

Finally, the use of topical retinoids mandates certain precautions. Retinoids are not only antineoplastic but also potentially tumor *promoters* in certain photocarcinogenesis assays.[9] This, plus phototoxicity due to possible retinoid-ultraviolet A interactions or a diminished generation of protein products of epidermal differentiation, can produce photosensitivity. Hence, the use of broad-spectrum sunscreens (a sun protective factor of 15 or higher) is indicated, which use will also help prevent a further progression of the deleterious effects of sunlight. Topical retinoic acid is also an irritant and therefore particularly difficult to administer to patients with "sensitive" skin—that is, those with atopy. Yet, with patience and careful follow-up, the poorly understood phenomenon of "hardening" occurs, allowing almost anyone to use this agent. Finally, the consequences of long-term usage in the elderly are not known, although some adolescents and young adults have used topical retinoic acid for decades without problems.

In the final analysis, it is the treating physician who must decide whether retinoids are indicated medically, cosmetically, or both—that is, when is one prescribing legitimately versus pandering to the wishes of patients simply shopping for the latest cosmetic angle. In the latter case, the risks may outweigh the potential benefits.

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Persistent Vaginitis

IN EVALUATING AND TREATING VAGINITIS and vaginal discharge, clinicians frequently face situations that are not straightforward.[1] Treatment choices often seem arbitrary, and failures occur. Confusion arises because of considerable variation in symptoms, coexistent infections, poor patient or partner compliance, and cultures that may not be specific.

Yeast Vaginitis

The organisms causing yeast vaginitis—*Candida albicans, Candida* species, and *Torulopsis glabrata*—can be identified in 10% to 30% of routine vaginal cultures because of high asymptomatic carrier rates.[2-4] Symptoms vary from minimal discomfort to intense itching or burning with associated vulvar erythema and abrasions. The vaginal discharge is scant to moderate, appears white and curdlike but may be thin and pasty, tends to adhere to vaginal walls, has no odor or smells musty, and has a pH of 4.0 to 5.0. A saline slide preparation shows a slight to a pronounced increase of leukocytes per high-power field. Adding potassium hydroxide shows mycelial forms. The highest yield will come from scrapings of vaginal sidewalls or the introitus.

The standard treatment of yeast vaginitis consists of applying miconazole or clotrimazole, 100 mg, to the vagina in